

## AMENDMENTS TO THE SPECIFICATION

**On page 1, please delete the following paragraph at line 9 (as entered in applicants' Preliminary Amendment, dated 24 September 2003) and replace it as shown:**

### **~~PRIORITY DATA~~**

~~This Application is a divisional of U.S. Patent Application No. 09/918,696, filed July 30, 2001, which claims priority from U.S. Provisional Application No. 60/222,887, filed August 3, 2000.~~

### **CROSS-REFERENCE TO RELATED APPLICATIONS**

This application is a divisional of U.S. Patent Application Serial No. 09/918,696, filed July 30, 2001, now U.S. Patent No. 6,635,244, which claims the benefit of U.S. Provisional Application Serial No. 60/222,887, filed August 3, 2000, now expired.

**On page 4, after line 13, please insert the following paragraphs:**

Accordingly, in one aspect, the present invention relates to a recombinant adenovirus comprising a mutation in the E1B-55K gene that encodes a mutated E1B-55K protein comprising a single amino acid mutation, the mutation substantially reducing the ability of the E1B-55K mutated protein to bind to the tumor suppressor p53. Examples of such recombinant adenoviruses include Onyx 051 and Onyx 053. The recombinant adenoviruses of may further comprise the property of substantially retaining late functions of the virus.

In a second aspect, the present invention relates to an isolated adenoviral E1B-55K protein comprising a single amino acid mutation wherein the mutation is selected from the group consisting of amino acids at positions 240 or 260 of the protein.

In a third aspect, the present invention relates to an isolated polynucleotide wherein the polynucleotide comprises mutated adenoviral DNA that encodes a E1B-55K protein, the protein comprising a single amino acid mutation which mutation substantially reduces the capacity of the protein to bind to the tumor suppressor, p53. In one embodiment of the invention, the isolated polynucleotide is RNA.

In a fourth aspect, the present invention relates to a method of treating cancer in a patient in need of the treatment, comprising administering to the patient a dose of a

recombinant adenovirus, the adenovirus comprising a mutation in the E1B-55K gene that encodes a mutated E1B-55K protein comprising a single amino acid mutation, the mutation substantially reducing the ability of the E1B-55K mutated protein to bind to the tumor suppressor p53, and allowing sufficient time for the adenovirus to infect the cancer, and repeating the treatment if desired. In one embodiment, the method may further comprise administering the recombinant adenovirus with a chemotherapeutic. Examples of the recombinant adenoviruses are Onyx 051 or Onyx 053.

In a fifth aspect, the present invention relates to a method of treating cancer in a patient in need of the treatment, comprising administering to the patient a dose of an isolated polynucleotide wherein the polynucleotide comprises mutated adenoviral DNA that encodes an E1B-55K protein, the protein comprising a single amino acid mutation which mutation substantially reduces the capacity of the protein to bind to the tumor suppressor, p53, and repeating the treatment if desired. In one embodiment, the isolated polynucleotide is RNA. In another embodiment, the isolated polynucleotide encodes the E1B-55K protein and the protein comprises a mutation at position 240 or position 260 of the protein. In yet another embodiment, the method may further comprise administering the polynucleotide with a chemotherapeutic. In one embodiment of the method, the polynucleotide is administered with a liposome.

**On page 4, at line 15, please insert the following paragraph:**

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.